

## CLAIMS

We claim:

1. A tagging-free method to detect binding of molecules, comprising the steps of:

(A) providing a sensor comprised of a first layer including a single stranded nucleic acid sequence and a second layer including a photoluminescent material;

(B) exposing said sensor to a biological sample for sufficient time for said single stranded nucleic acid sequence to bind to a material of interest in said biological sample;

(C) exposing said sensor to light and measuring photoluminescence from said sensor.

2. The tagging-free method of claim 1, wherein the single stranded nucleic acid is selected from the group consisting of DNA, RNA and PNA.

3. The tagging-free method of Claim 1 wherein said second layer is selected from the group consisting of aromatic polymers, doped or undoped metal oxides, sulfides, selenides, arsenides, tellurides, and nitride and phosphide nanocomposites.

4. The tagging-free method of claim 1 wherein said second layer comprises a matrix material, with said photoluminescent material associated with said matrix material.

5. The method of claim 4 wherein said photoluminescent material is embedded in said matrix material.

6. The tagging-free method of claim 1, wherein the second layer comprises polystyrene.

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Sub A1

Sub A2

Sub C3

Sub C4

8. The tagging-free method of claim 7, wherein the photoluminescent particles are doped or undoped compounds selected from the group consisting of group II and group VI.

10. The tagging-free method of claim 1, wherein the second layer comprises a nanocomposite.

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12. The tagging-free method of claim'11, wherein the wavelength of the ultraviolet light applied is in the range of 260-265 nm.

13. The tagging-free method of claim 1, wherein the first layer comprises an ssDNA monolayer.

14. The tagging-free method of claim 1, wherein the second layer comprises a thin-film or a support.

15. The tagging-free method of claim 1, wherein the second layer comprises a polymer.

16. The tagging-free method of claim 1, wherein the nucleic acid sequence is between 5 and 200 base pairs.

Variable	Mean	Standard Deviation	Minimum	Maximum
Age	34.5	10.2	22	55
Gender	0.5	0.5	0	1
Marital Status	0.6	0.5	0	1
Education	12.5	1.5	10	15
Income	3500	1500	1000	7000
Health	0.8	0.2	0	1
Smoking	0.3	0.5	0	1
Alcohol	0.2	0.4	0	1
Exercise	0.4	0.5	0	1
Stress	0.6	0.5	0	1
Depression	0.1	0.3	0	1
Loneliness	0.3	0.5	0	1
Life Satisfaction	0.7	0.4	0	1
Quality of Life	0.8	0.3	0	1
Overall Health	0.9	0.2	0	1
Physical Health	0.9	0.2	0	1
Mental Health	0.8	0.3	0	1
Social Health	0.7	0.4	0	1
Emotional Health	0.6	0.5	0	1
Behavioral Health	0.5	0.5	0	1
Environmental Health	0.4	0.5	0	1
Occupational Health	0.3	0.5	0	1
Financial Health	0.2	0.4	0	1
Family Health	0.1	0.3	0	1
Community Health	0.0	0.2	0	1
National Health	0.0	0.1	0	1
Global Health	0.0	0.0	0	1

17. The tagging-free method of claim 16, wherein the sequence is about 25 base pairs.

18. The tagging-free method of claim 17, wherein the second layer has fluorescence when excited by light with a wavelength in the 200-700 nm range.

19. The tagging-free method of claim 1, wherein the sensor comprises ssDNA as said first layer grafted onto the second layer.

20. The tagging-free method of claim 1, including providing a discontinuous first layer comprising different nucleic acid sequences in different sections of said first layer.

21. The method of claim 1, wherein said first layer is positioned on a first side of said second layer, and said measuring step measures photoluminescence from a second side of said second layer.

22. The method of claim 21, wherein said second side is opposite said first side on said second layer.

23. The method of claim 1, wherein said first layer is positioned on a first side of said second layer, and said measuring step measures photoluminescence reflected from said first side of said second layer.

24. An apparatus for tagging-free detection of binding of molecules, comprising:

- a light source;
- a sensor having a nucleic acid layer and a photoluminescent layer; and
- a photoluminescence detector.

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25. The apparatus of claim 24, wherein the light source is an ultraviolet light source.

26. The apparatus of claim 24, wherein the light source is an infrared light source.

27. The apparatus of claim 24 wherein the light source is a visible light source.

28. The apparatus of claim 24 wherein the detector is a light detector in the infrared to ultraviolet range.

29. The apparatus of claim 28 wherein the light source is a visible light source.

30. The apparatus of claim 25, wherein the ultraviolet light source provides ultraviolet light at a range of about 260-265 nm.

31. A method of making a tagging-free sensor, comprising:  
contacting a single stranded nucleic acid sequence with a photoluminescent material.

32. The method of claim 31, including depositing photoluminescent material on a substrate to form a surface, and thereafter modifying the surface by ion exchange treatment with a metal salt, followed by ion-embedding, followed by exposing the ion-embedded material to reactive media to form photoluminescent particles.

33. A tagging-free sensor comprising a first layer including a single stranded nucleic acid sequence and a second layer including a photoluminescent material.

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35. The sensor of claim 33, wherein said second layer is selected from the group consisting of aromatic polymers, metal oxides and sulfides, and nanocomposites.

37. The sensor of claim 33, wherein the second layer comprises zinc sulfide.

39. The sensor of claim 33, wherein the nucleic acid sequence is about 25 base pairs.

40. The sensor of claim 33, wherein the first layer comprises an ssDNA monolayer.

41. The sensor of claim 33, wherein the second layer is made from material that fluoresces when excited by radiation in the UV region.

42. A tagging-free method to detect binding of antigens, comprising the steps of:

(A) providing a sensor comprised of a first layer including an antibody and a second layer including a photoluminescent material;

(B) exposing said sensor to a biological sample for sufficient time for said antibody to bind to an antigen of interest in said biological sample;

(C) measuring photoluminescence from said sensor.

43. The tagging-free method of claim 42, including photoluminescent measurement of light reflected from the second layer when ultraviolet light with wavelength in the range of 200-700 nm is applied to the first layer.

44. The tagging-free method of claim 43, wherein the wavelength of the ultraviolet light applied is in the range of 260-265 nm.

45. The tagging-free method of claim 42, wherein the second layer fluoresces when excited by ultraviolet radiation.

46. The tagging-free method of claim 42, wherein the first layer is discontinuous and comprises different antibodies.

47. An apparatus for tagging-free detection of antibody binding, comprising:

- a light source;
- a sensor having a first layer including an antibody and a second photoluminescent layer; and
- a light detector.

48. A tagging-free sensor comprising a first layer including an antibody and a second layer including a photoluminescent material.

49. The sensor of claim 48, wherein the first layer is discontinuous and comprises different antibodies.

50. The sensor of claim 49, including different known antibodies.

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